IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	Nadeson et al.	Confirmation No.	9722
Serial No.:	10/574,438	Group Art Unit:	1614
Filing Date:	06/25/2007	Examiner:	Jagoe, Donna

Title: METHODS AND COMPOSITIONS

DECLARATION OF COLIN GOODCHILD UNDER 37 C.F.R. § 1.132

I, Colin Goodchild, hereby declare as follows:

1. I am an inventor on US Patent Application No. 10/574,438. I have been briefed by patent counsel in respect of the Office Action issued from the US Patent and Trademark Office on February 2, 2010. In the Official Action, the Examiner has alleged that the claims lack an inventive step in light of Nickel *et al.* (*Regional Anesthesia and Pain Medicine*, 18:4, 1993) and Grond *et al.* (*Pain* 79:15-20, 1999).

2. The following experiments were conducted by me, or under my supervision, and demonstrate the efficacy of treating neuropathic pain using a therapeutic combination of flupirtine and an opioid. Two animal models in which the animals have neuropathic pain were tested.

3. The first is the streptozotocin (STZ)-induced diabetic neuropathy model. In these experiments, rats were injected i.p. with STZ (150 mg/kg total dose) dissolved in 0.9% sodium chloride solution. The induction of diabetes was confirmed 1 week after injection of STZ by measurement of tail vein blood glucose levels. The rats were tested for hyperglycemia once per week to confirm continued high blood glucose readings.

4. Hyperalgesia was assessed using the paw pressure test. Paw pressure was measured using a Ugo Basile algesimeter (Apelex; probe 1mm, weight 10g). Increasing pressure was applied to the left hind paw until vocalization or sharp paw withdrawal was elicited. Paw withdrawal thresholds were measured for a group of weight matched controls and also in drug treatment groups of rats, 20 and 10 minutes before, immediately before (time 0), and also at 20, 30, and 40 minutes after i.p. injections of:

-saline (controls);
-flupirtine 5mg/kg;
-flupirtine 10 mg/kg;
-morphine 1.6 mg/kg;
-morphine 3.2 mg/kg;
-flupirtine 5 mg/kg plus morphine 3.2 mg/kg; or
-flupirtine 10 mg/kg plus morphine 1.6 mg/kg.

5. Tests took place 5 weeks after the first injection of STZ. Animals that had paw pressure nociceptive thresholds below 30 g (60% of the value of weight matched normal controls) were deemed to have developed hyperalgesia/neuropathic pain and thus used in further experiments.

6. In these studies, morphine when administered alone at a dose of 3.2 mg/kg resulted in no significant antinociception. However, a lower dose of morphine (1.6 mg/kg shown to be ineffective when administered alone) given in combination with flupirtine at 10 mg/kg caused highly significant antinociceptive effects causing complete reversal of hyperalgesia caused by diabetic neuropathy ($P < 0.001$, one-way analysis of variance). This combination of drugs was not sedating. As can be seen in Figure 1 (***attached***), the effects are not merely additive.

7. Male Wistar rats (HsdBrlHan WIST strain, 100-200g) were anaesthetized with halothane and syngeneic prostate cancer cells (AT3B-1 prostate cancer) were injected into the medullary cavity of the tibia. This led to an expanding tumor within the bone 2-3 weeks following injection. These changes were accompanied by the development of hyperalgesia to heat applied to the ipsilateral hind paw in 75% of rats treated.

8. The maximum non-sedating doses of morphine and flupirtine given alone and in a 4:1 dose combination were defined using open field activity monitor. Saline and gabapentin (100mg/kg i.p.) controls were also included in the studies. The rats were placed individually in an open field activity which is a darkened box in which the movement of the rat can be monitored remotely by the frequency and number of interruptions of infrared beam directed across the box in a grid. The activity of the monitor was measured for a period of 20 minutes in each rat after the administration of the drug(s) or saline control. If a rat was sedated by a drug treatment, the movements recorded would be less than the saline controls.

9. Paw withdrawal thresholds from noxious heat were measured. Dose response curves were plotted for morphine (0.312-10 mg/kg) and flupirtine (1.25-10 mg/kg i.p.) given alone and also for drugs given together in a 4:1 flupirtine:morphine fixed dose ratio combination (total dose 0.156-5 mg/kg i.p.). The responses were subjected to linear regression of log dose/response curves with subsequence isobolographic analysis.

10. The maximum non-sedating doses of morphine alone, flupirtine alone and 4:1 fixed dose ratio were 10, 8 and 4 mg flupirtine: 1mg morphine respectively. Non-sedating doses of both morphine (ED50=0.735 mg/kg) and flupirtine (ED50=3.317 mg/kg) as well as the fixed dose combination (ED50=0.39 mg/kg) caused dose related antinociception (see Figure 2, ***attached***). Isobolographic analysis revealed that there was a synergistic interaction between flupirtine and morphine (see Figure 3, ***attached***).

11. Therefore, the data demonstrate that the same amount of analgesia could be achieved with a combination of flupirtine and morphine (4:1) as could be achieved using the drugs alone, but with 10% of the ED50 doses of each drug in the fixed dose combination. These results demonstrate that flupirtine in combination with an opioid allows a significant reduction in the amount of either drug administered alone in order to obtain an analgesic effect. Therefore, the use clinically of the combination of flupirtine and an opioid in the treatment of neuropathic pain provides enhanced therapeutic management of pain and disease and allows the administration of lower levels of drugs, thereby decreasing the associated side effects.

12. The results of these studies demonstrate that the analgesic effect of the combination of flupirtine and an opioid is synergistic when compared to the use of either compound alone.

13. The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information are believed to be true, and further that these statements were made with the knowledge that willful, false statements, and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Date:_____

_____
COLIN STANLEY GOODCHILD

Figure 1: STZ-induced diabetic rat neuropathic pain model

A combination of flupirtine and morphine, exhibits significantly greater antinociceptive effects without sedation than either drug alone. The combination of flupirtine and morphine also exhibits significantly greater antinociception without sedation when compared to the current clinical "gold standard" therapies, including gabapentin

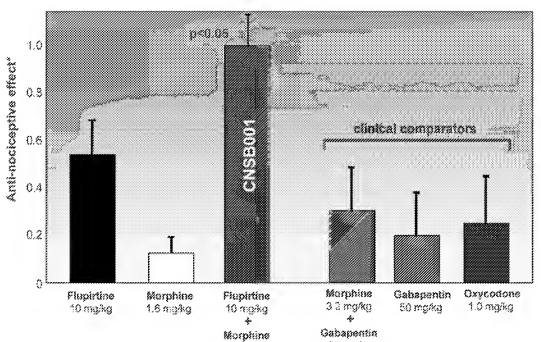


Figure 2: Rat bone cancer model

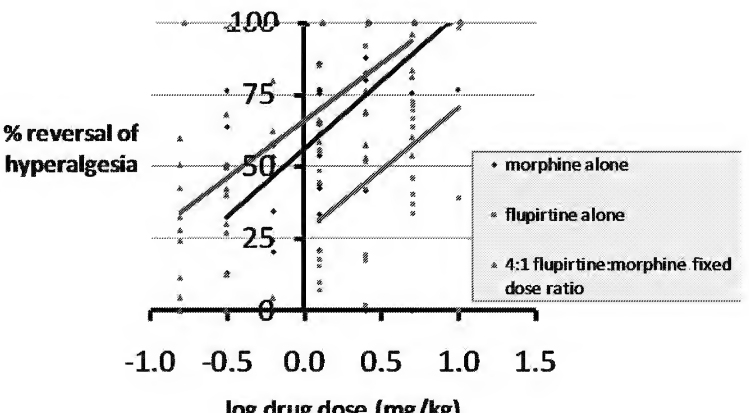
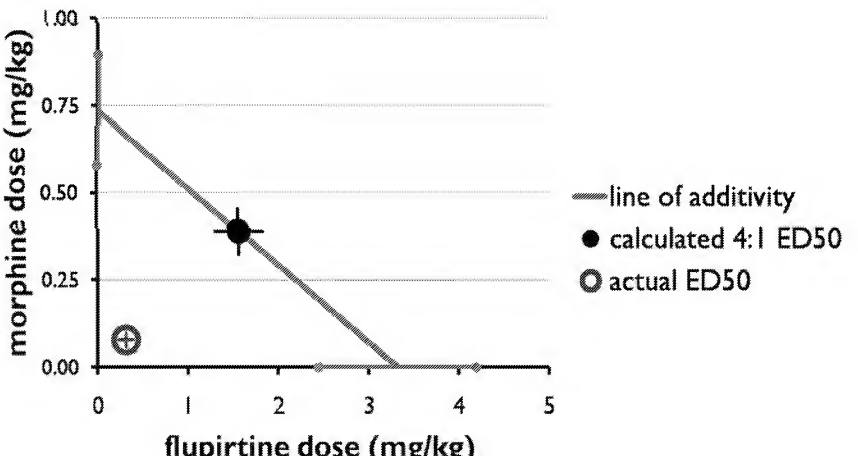


Figure 3: Rat bone cancer model



COLIN STANLEY GOODCHILD

MA., MB. BChir., PhD., FRCA., FANZCA., FFPMANZCA..
Academic Specialist in Anaesthesia and Pain Medicine

Summary

The career details enclosed in this document show that I am a very experienced and qualified clinician in the fields of anaesthesia and pain medicine. I have practised in several countries in Europe and also in Australia. In addition I am a trained and qualified basic scientist. I have combined these skills and interests in developing an academic career pursuing neuroscience and clinical research side by side. I have written many papers, published in major international journals and have taught and presented my research all over the world. I have set up a new academic department and am thus no stranger to administration. I have experience of the pharmaceutical industry, at first with collaborative clinical research, but more recently with drug development. I have been successful in taking my intellectual property through development in the laboratory, proof of concept in humans and patenting. I have a blend of clinical and basic scientific skills and experience combined with good experience of clinical pharmacology.

Colin Goodchild

Saturday, 24 April 2004

DATE OF BIRTH 8th May 1949

NATIONALITY British

MARITAL STATUS Married, 2 children

PROVIDER NUMBER 2032621T

MEDICAL BOARD REG. 26128 Victoria

MEDICAL EDUCATION

Pre-clinical: Kings' College, Cambridge 1967-1971

Clinical: St. George's Hospital,
University of London 1971-1974

Academic Qualifications: M.A. (Cantab) December 1973
M.B., B.Chir. June 1974
F.R.C.A. (Eng) February 1978
Ph.D. (University of Leeds) September 1984
F.A.N.Z.C.A. 1994
F.F.P.M.A.N.Z.C.A. 2000

Research Administration: National Health & Medical Research Council Aust. grant referee 1996-
National Health & Medical Research Council N.Z. grant referee 1995-
National Health & Medical Research Council Singapore 1999 -
British Journal of Anaesthesia referee 1993 -
Anesthesia and Analgesia referee 1999 –
National Assessors Panel for Cancer Research Grants - 1995

Memberships: Australian Pain Society 1993 -
International Association for the Study of Pain 1990-
Anaesthetic Research Society (UK) 1985 -
Australasian Society of Clinical for Experimental Pharmacology and Toxicology 1998 –
Asean and Oceanic Society of Regional Anaesthesia 1999 -
International Anesthesia Research Society 1999-
European Academy of Anesthesiology (now EAA) 1995 -

ACADEMIC APPOINTMENT

January 1993
Foundation Professor of Anaesthesia
Monash University, Melbourne, Victoria

OTHER APPOINTMENTS

Senior Editor of the Journal "Pain Medicine"

Chief Scientific Officer CNSBio Pty Ltd

HOSPITAL APPOINTMENTS

1993
Visiting Medical Officer, Southern Health Care Network

1993
Visiting Medical Officer, Peninsula Health Care Network

1996
Visiting Specialist, John Fawkner Hospital

February 1999
Visiting Specialist, Cabrini Hospital

March 2000
Visiting Specialist, Epworth Hospital

April 2000
Visiting Specialist, South Eastern Private Hospital

PREVIOUS APPOINTMENTS

Pre-registration:

July 1974 - January 1975
House Physician in General Medicine and Dermatology,
St. George's Hospital, London.

February 1975 - August 1975
House Surgeon in General Surgery,
Thanet District Hospital, Margate.

Post-registration:

August 1975 - November 1976
Senior House Officer in Anaesthetics,
St Mary's Hospital, Portsmouth.

November 1976 - March 1977
Senior House Officer in Anaesthetics,
Southampton General Hospital.

April 1977-March 1979
Registrar in Anaesthetics,
Southampton General Hospital.

April 1979 - March 1982
Wellcome Research Fellow,
Department of Cardiovascular Studies,
University of Leeds.

April 1982 - August 1982
Locum appointments, including four months

as Locum Anaesthetic Specialist in
Eudokia Ziekenhuis, Rotterdam, The Netherlands.

September 1982 - January 1984
Senior Registrar, Hammersmith Hospital and
Honorary Tutor,
Royal Postgraduate Medical School, London.

February 1984 to December 1992
Senior Lecturer in Anaesthesia,
University of Leeds,
Honorary Consultant Anaesthetist,
The General Infirmary at Leeds.

CURRENT APPOINTMENT

academic

I was appointed Foundation Professor in the new Monash University Department of Anaesthesia in 1992. I took up my appointment in Australia in January 1993. This is the first University Chair of Anaesthesia in the State of Victoria. I have built up the Department from scratch with the broad brief from the College of Anaesthetists, the Victorian Chairs of Anaesthesia Appeal and Monash University to increase the status and profile of academic anaesthesia in the State of Victoria. The major thrust of this work involves teaching and research as well as public relations. After my arrival I immediately began the task of getting the Department up and running with respect to administration. Having appointed a secretary and established the basic administrative bones of the Department I set about my main task, which was commissioning a basic research laboratory in order to continue my work, started in Leeds; basic scientific studies of antinociceptive mechanisms. I appointed a Research Fellow who has a PhD from Monash University Department of Pharmacology and we began work together on spinally administered analgesics in rats as I had done in Leeds. This field of endeavour has been very productive with many abstracts presented to national and international meetings and papers published in Journals such as Pain, Journal of Pharmacology and Experimental Therapeutics, Anesthesiology and British Journal of Anaesthesia. Most of the research in the Department has been based in this laboratory but some clinical research has been completed in Monash Medical Centre. Some of this such as studies in postoperative analgesia with dextromethorphan and the new local anaesthetic, ropivacaine were in close collaboration with pharmaceutical companies.

The Department is involved extensively in undergraduate as well as postgraduate teaching. This includes teaching of undergraduates in anaesthesia and postoperative pain relief during their 5th year, postgraduate anaesthetic lectures at Hospital and at College level as well as invited lectures in Melbourne as well as outside the City of Melbourne in the State of Victoria.
I have created further academic positions in the University Department at the level of lecturer. These individuals are anaesthetists in clinical training whom also research and study within the Department for the degree of PhD. At the end of their five-year appointment, the lecturers emerge fully qualified Consultant Anaesthetists with a basic science PhD training. Two have already done so with PhD training in basic science. Another fully qualified anaesthetist has finished study in the department and has been awarded the degree of PhD. Her studies involved molecular biology of $GABA_A$ receptors at the level of the spinal cord.

It can be seen that the University Department of Anaesthesia at Monash has basic science and teaching interests in the field of pain. I am very involved in the provision of the Acute Postoperative Pain Service at Monash Medical Centre and I have also helped set up a pain clinic in Southern Health which provides pain medicine services for patients with chronic non malignant pain and also cancer associated pain. In addition to being granted the Australian and New Zealand College of Anaesthetist diploma (ANZCA), I have been elected as a fellow to the newly formed Faculty of Pain Medicine (FFPMANZCA). My teaching and research interests span the full range encompassed by pain medicine: from molecular pharmacology of $GABA_A$ receptors involved in spinal cord pain processing; through studies in whole animals with acute and chronic pain models with analgesic drugs acting at the level of the spinal cord; to clinical work with patients suffering from acute and chronic pain states. This has been extended further in recent years with another lecturer whose research involves work on pain epidemiology. In particular we are looking at the effect on quality and type of acute pain management on subsequent incidence of chronic pain.

Grants and donations from the following sources have financed the work of the department:

- Australian and New Zealand College of Anaesthetists
- Australian Society of Anaesthetists
- National Health and Medical Research Council
- Southern HealthCare Network
- Tattersalls
- Harold and Cora Brennan Trust
- FH Faulding
- ICI
- Astra
- Zeneca
- Purdue Pharma

Drug Discovery and Development

Research on spinal cord $GABA_A$ receptors that began in Leeds in 1985 led to discovery of a number of subtypes of these receptors involved in spinal cord control of antinociception. I proved clinically with midazolam that drugs acting at these receptors could be very potent analgesics in humans. However midazolam had to be injected intrathecally, directly into the cerebrospinal fluid; this is invasive and a specialised treatment but it is useful and in regular clinical use in a number of places around the world. It occurred to me then that these $GABA_A$ receptors might be sufficiently different to be targeted selectively by compounds that would be novel analgesics. Preliminary experiments with water-soluble neurosteroids showed that this group of drugs could interact with spinal cord $GABA_A$ receptors to produce analgesia without sedation. I have since proved that orally administered neurosteroid can cause powerful antinociception by action at those spinal cord $GABA_A$ receptors. This action is so specific that the pain reliving effects are produced without effects on the brain such as sedation. This has been translated to humans; a drug taken orally potentiates opioid analgesics without increased sedation or nausea. This culminated in the patenting of neurosteroids for use as analgesics. I took the drug through the patenting process working directly with patent attorneys. I also organised meetings and negotiations to license the technology to an industry partner. The formal commercial development process of my intellectual property is now under way. I am still involved with the decision making process in that project. The latter has been an interesting and stimulating experience that has led to my interest in entering the drug development and commercialisation industry. I have come to realise that I have a unique blend and breadth of scientific, academic, clinical and administrative experience that combine well in this sort of activity.

Clinical

I maintain an active clinical anaesthetic involvement providing clinical anaesthesia for a total of two days and one night on call per week serving a variety of surgical specialties including general surgery, orthopaedics, thoracic surgery, urology, gynaecology and obstetrics and plastic surgery. I run the acute pain relief service in Monash Medical Centre where I am the main referral and information source for senior and junior doctors seeking help and information in the conduct of all aspects of pain medicine.

I have also been involved with the work of Monash Medical Centre therapeutics committee. I was its chairman for five years, and I oversaw its transition to the committee for all the hospitals in the Southern HealthCare Network. My standing in the profession often leads to me being asked for my professional opinion on the conduct of a patients treatment for use in legal proceedings.

CLINICAL EXPERIENCE

Pre-registration

My first clinical appointment as House Physician in General Medicine was held at my teaching hospital, St. George's, Hyde Park Corner. I was responsible for patients under the care of Professor Dornhorst and two dermatology teams.

General Professional Training

I started my postgraduate education in anaesthetics in St. Mary's Hospital, Portsmouth, and after one year in this appointment I passed my Primary F.F.A. examination. I was trained to anaesthetize patients for a variety of surgical procedures, both elective and acute. I also became interested in local anaesthetic techniques, particularly epidural and spinal anaesthesia.

I was appointed Registrar in Anaesthesia at Southampton General Hospital in 1977. I added to my experience of anaesthesia for general, ENT, ophthalmic and gynaecological surgery and obstetrics. In addition I received training in anaesthesia for neurosurgery, cardiac and thoracic surgery and paediatric surgery. This was an excellent scheme for General Professional Training and I was successful at the Final F.F.A. examination in February 1978.

During my final year as a Registrar in Southampton General Hospital I gained further experience, performing many duties of the senior registrars. This included another training module of three months in cardiac and thoracic anaesthesia. This incorporated paediatric open and closed heart operations and thoracic surgical procedures such as pneumonectomy, lobectomy, thymectomy and surgery for pectus excavatum.

Higher Professional Training

After my locum specialist appointment in anaesthesia in Rotterdam I was appointed Senior Registrar in Anaesthesia in the Hammersmith Hospital. There I gained further training in anaesthesia for many branches of surgery that included cardiothoracic (open and closed heart procedures in adult and paediatric patients as well as thoracotomy for lung surgery), major hepatobiliary surgery and intensive care. During this appointment I confined my activities to clinical duties and completion of my Ph.D. thesis. However, while working in the Hammersmith Hospital one could not fail to be attracted by the productive co-existence of clinical duties and research interests. I decided to return to academic activities after completing my higher professional training.

Clinical duties during previous appointment

My previous appointment of Senior Lecturer in Anaesthesia in the University of Leeds carries an honorary consultant contract with the Leeds Western Health Authority. When I began this appointment I gave anaesthetics to patients on three surgical lists: two general surgical lists involving major colorectal surgery and one orthopaedic surgical list. I also took part in the general consultant on-call rota (one or two nights on-call per month, and one weekend every two months).

Many changes occurred after Professor McDowall's death in December 1984. Besides my own clinical commitments I managed some of Professor McDowall's clinical responsibilities; in particular, I gave anaesthetics for a whole day general surgical list. The responsible surgeon was Professor David Johnston and patients underwent major colorectal procedures including mucosal proctocolectomies (the surgery sometimes lasted up to 12 hours).

My clinical duties up to April 1991 were two all-day surgical lists:

1) With Professor David Johnston -general surgery;
2) a cardiothoracic surgery list.

These were both very heavy surgical lists lasting at least 8 hours each. A combination of these two commitments provided me with the best possible material to maintain my clinical skills.

Besides the general surgical procedures such as anterior resections, hemicolectomies and gastric surgery, I also gave anaesthesia for longer procedures such as the mucosal proctectomies with total colectomies. This involved a wide range of practical skills such as arterial and central venous catheterisation and regional anaesthesia: subarachnoid; epidurals both lumbar and thoracic. My cardiothoracic list involved adult open and closed heart operations and also thoracotomies for lung surgery.

It was and still is my practice to offer thoracic epidural analgesia to my patients undergoing major intra-abdominal and thoracic surgery. This technique provides postoperative analgesia using a mixture of epidural bupivacaine and opioid for a period up to 72 hours. I developed a technique for postoperative analgesia using intrathecal midazolam and diamorphine while working in Leeds. This development extended from my laboratory research. I have continued to use this method although the opioid has changed to morphine because of availability. I have taught and promulgated the technique for management of acute and chronic pain states (including cancer) for fifteen years. It is now used in many centres around the world. The method produces excellent analgesia without the side effects that we see with the epidural technique and thus is particularly suitable fo sicker, high risk, patients.

RESEARCH TRAINING AND EXPERIENCE

Studies for the Degree of Ph.D.

After gaining my final F.F.A. one year into my Registrar appointment at Southampton, I became interested in making physiological measurements in patients under anaesthesia and in intensive care. It soon became obvious to me and to the Professor of Anaesthesia (Professor John Norman) that I needed proper training in research methods, philosophy and techniques. I joined the Department of Cardiovascular Studies in Leeds in 1979 as Wellcome Research Fellow for three years full-time research. During my three years in the Department of Cardiovascular Studies I carried out original research in cardiovascular physiology and neurophysiology under the guidance of Professor R.J.Linden and Dr Cecil Kidd (later Regius Professor of Physiology at the University of Aberdeen).

My Ph.D. thesis is entitled "The Brain Stem and Spinal Cord Pathways involved in the Left Atrial Stretch Reflex", and my Ph.D. project consisted of three separate studies.

a) The purpose of the first section was to determine the intraspinal distribution of neurones contributing impulses to the renal sympathetic nerves. The reason for this was to define the area of spinal cord that should be explored neurophysiologically for neurones responding to left atrial stretch receptor stimulation; stimulation of these receptors inhibits renal nerve activity. I made a detailed anatomical study of the sympathetic nervous system defining the intraspinal distribution of sympathetic preganglionic neurones and the intraspinal origin of renal nerve activity. This required maintaining dogs in good physiological condition under anaesthesia for extended periods (up to 72 hours) while waiting for the active transport of horseradish peroxidase to the cell bodies of sympathetic preganglionic neurones within the spinal cord.
The histochemical and histological procedures were all performed by me; by using the very sensitive tetramethylbenzidine technique I was able to follow the intraspinal course of axons and dendrites of labelled neurones more extensively than had been demonstrated before. Several aspects of this work have been presented to anatomical and physiological societies and the completed work has been published as a full paper. It was concluded that most preganglionic neurones contributing activity to the renal nerves were located in spinal cord segments T10, 11 and 12.

b) The aim of the main study was to define specifically the types of responses and the anatomical distribution in the medulla oblongata and spinal cord, of neurones whose activity was altered by left atrial receptor stimulation. I made electrophysiological recordings of the spontaneous activity of single neurones in the medulla oblongata and spinal cord of the dog while stimulating atrial receptors. This complex preparation involving cardiovascular and neurophysiological techniques was demonstrated to the Physiological Society. I concluded that inhibition as well as excitation of neuronal activity by atrial stretch receptor stimulation occurred not only in the area of spinal cord responsible for renal nerve activity but also in the medulla oblongata.

c) My electrophysiological experiments required detailed anatomical marking of electrophysiological recording sites. These sites were mapped out precisely by iontophoresis of dye from the tip of a new gold sputter-coated micropipette which I developed for this purpose. Details of electrode manufacture have been demonstrated to the Physiological Society, and the method has also been published as a paper.

As well as working on my own projects I collaborated with a colleague, Dr J.A.Bennett, in his work on cat medulla oblongata, making electrophysiological recordings of single neurones in the brain stem of the cat that were excited or inhibited by electrical stimulation of one or more different branches of the vagus nerve.

My thesis was completed during my appointment as Senior Registrar in Anaesthesia in the Hammersmith Hospital and I was awarded the degree of Ph.D. from the University of Leeds in September 1984.

Independent Research

I always intended to use my research training and experience gained in the Department of Cardiovascular Studies in the pursuance of a career in research. In particular I have always felt that much is to be gained by the application of basic science disciplines to problems in anaesthesia and pain medicine. I realised that the neurophysiological and anatomical techniques that I had learned during my Ph.D. training would be useful in research directed towards the understanding of the handling of nociceptive information by the dorsal horn of the spinal cord. Such knowledge would be useful in the design of treatments for both postoperative and persistent pain states.

Upon taking up my appointment in Leeds my brief from Professor McDowall was to become an independent researcher working in the new and then uncommissioned anaesthetic department laboratory in the new Medical and Dental School in Leeds. The new laboratory was equipped and I was able to perform acute and recovery experiments in the fields of neurophysiology, neuropharmacology, neuroanatomy and cardiovascular physiology on a variety of animals.

My laboratory research interests have been in the following areas.

a) Cardiovascular studies: to define the mechanisms by which anaesthetic drugs affect the circulation. Central to these studies is the use of laboratory preparations that divorce the cardiovascular effects mediated by depression of central sympathetic nervous system outflow by anaesthetic drugs and their direct action on the heart and blood vessels. From studies on the dog and on isolated tissues, we have concluded that direct venodilator and arteriolar vasodilator effects contribute to the greater cardiovascular depression of some intravenous anaesthetic agents.

b) Spinally administered analgesics: to define the effect of potential analgesic substances given spinally and to define their basic mechanisms of action. The work has involved the development of an animal model that allows the demonstration of segmental analgesic effects following intrathecally administered drugs, as well as neurophysiological and neuropharmacological investigations, on neuronal activity in the spinal cord.

I have also performed investigations in humans in the operating theatre and in the pain clinic. Thus it is possible to investigate the antinociceptive actions of a drug in the laboratory using several different approaches leading to a fundamental understanding of the mechanisms involved in those actions, and subsequently to investigate the clinical usefulness of the drug. The drugs investigated so far include opioids and benzodiazepines (including midazolam) as well as steroid anaesthetics, propofol, 5HT and cholinergic receptor and adrenoceptor agonists. Results from this research programme have been presented to the Anaesthetic Research Society on several occasions, the Pharmacological Society, the European Academy of Anaesthesiology, the British Opioid Colloquium and the International Association for the Study of Pain.

The work on intrathecal midazolam involved collaboration with Dr J.M.Serrao after her appointment as Lecturer (Honorary Senior Registrar) in the University Department of Anaesthesia. After our initial experiments, Dr Serrao registered for the degree of Ph.D. with the University of Leeds. The subject matter for the thesis was to be the analgesic effects of spinally applied substances, in particular, the benzodiazepines. The work involved neuropharmacological experiments in the laboratory and clinical experiments in the operating theatre and pain relief clinic. Collaboration with the Department of Pharmacology in the University of Leeds led to the formation of the Spinal Analgesia Group.

Since then much work was performed while I was in Leeds, not only with Dr Serrao, but also with other postgraduates, Ph.D. students and eight undergraduates during the last four years of my

appointment in Leeds. I supervised undergraduate pharmacology students in their final year research projects; in 1991 four of these students worked on various aspects of spinal antinociceptive mechanisms.

Other Clinical Research

I also collaborated with the University Department of Medicine in Leeds on two projects investigating the effects of the plasma expander, hydroxycthyl starch, and the serum protease inhibitor, aprotinin, on haemostatic mechanisms and post-operative blood loss. The latter study was a large double blind study of haemostasis and post-operative blood loss in patients having repeat surgery for replacement of heart valves. The haemostatic effect of aprotinin is potentially an important economic factor as well as increasing the safety of this highly complex operative procedure. The results have now been published. Aprotinin does cause a statistically significant reduction in postoperative blood loss but this may be clinically and economically unimportant. The results indicate that a full cost/benefit and risk analysis of the causes of operative blood loss and it's treatment is indicated.

PUBLICATIONS

Papers published:

Bennett JA, Goodchild CS, Kidd, C, McWilliam PN. The excitation of neurones in the brain stem by vagal afferent fibres from the heart and lungs. Journal of Physiology 369: 1-15; 1985

Bennett JA, Goodchild CS, Kidd, C, McWilliam PN. The location and characteristics of sympathetic preganglionic neurones in the lower thoracic spinal cord of the dog and cat. Quarterly Journal of Experimental Physiology 71: 79-92; 1986

Goodchild CS, Crane R, Bennett JA, Ford TW, Kidd C, McWilliam PN. A sputtered gold microelectrode in combination with a multibarrelled micropipette: a low impedance extracellular recording electrode with the facility for iontophoresis. Electroencephalography and Clinical Neurophysiology 67: 91-94; 1987

Goodchild CS, Noble J. The effects of intrathecal midazolam on sympathetic nervous system reflexes in man - a pilot study. British Journal of Clinical Pharmacology 23: 273-285; 1987

Goodchild CS, Serrao JM. Intrathecal midazolam in the rat: evidence for spinally-mediated analgesia. British Journal of Anaesthesia 59: 1563-1570; 1987

Cripps TP, Goodchild CS. Intrathecal midazolam and the stress response to upper abdominal surgery: adrenocortical, glycaemic and analgesic effects. Clinical Journal of Pain 4: 125-128; 1988

Goodchild CS. Post-operative recovery rooms: staffing and facilities in three regions in the United Kingdom. Anaesthesia 43: 829-832; 1988

Bennett JA, Goodchild CS, Kidd, C, McWilliam PN. Inhibition of brain stem neuronal activity by cardiac and pulmonary vagal afferent fibres in the cat. Quarterly Journal of Experimental Physiology 73: 959-972; 1988

Bell DB, Goodchild CS. Hypertrophic obstructive cardiomyopathy in combination with a prolapsed mitral valve. Anaesthesia for surgical correction with propofol. Anaesthesia for surgical correction with propofol. Anaesthesia 44: 404-411; 1989

Serrao JM, Stubbs SC, Goodchild CS, Gent JP. Intrathecal midazolam and fentanyl in the rat: evidence for different spinal antinociceptive effects. Anesthesiology 70: 780-786; 1989

Goodchild CS, Serrao JM. Cardiovascular effects of propofol in anaesthetized dog. British Journal of Anaesthesia 63: 87-92; 1989

Weir DL, Graham DI, Goodchild CS. Propofol: Effects on indices of cerebral ischaemia. Journal of Neurological Anesthesiology 1989, Vol 1, pt III.

Bentley GN, Gent JP, Goodchild CS. Vascular effects of propofol: smooth muscle relaxation in isolated veins and arteries. Journal of Pharmacy and Pharmacology 41: 797-798, 1989
Serrao JM, Mackenzie JM, Goodchild CS, Gent JP. Intrathecal midazolam in the rat: an investigation of possible neurotoxic effects. European Journal of Anaesthesiology 7: 115-122, 1990

Lowson S, Gent JP, Goodchild CS. The anticonvulsant properties of propofol and thiopentone: A comparison using two tests in laboratory mice. British Journal of Anaesthesia 64:59-63, 1990

Edwards M, Serrao JM, Gent JP, Goodchild CS. On the mechanism by which midazolam causes spinally-mediated analgesia. Anesthesiology 73: 273-277; 1990.

Goodchild CS, Sanghera S, Serrao JM, Gent JP. Analgesia mediated by spinal kappa opioid receptors. European Journal of Anaesthesiology 8: 227-231; 1991.

Lowson S, Gent JP, Goodchild CS. Convulsive thresholds in mice during the recovery phase from anaesthesia induced by propofol, thiopentone, methohexitone and etomidate. British Journal of Pharmacology 102: 879-882, 1991.

Serrao JM, Goodchild CS, Gent JP. Reversal by naloxone of spinal antinociceptive effects of fentanyl, ketocyclazocine and midazolam. European Journal of Anaesthesiology 8:401-406, 1991.

Boulter N, Serrao JM, Gent JP, Goodchild CS. Spinally-mediated antinociception following intrathecal chlordiazepoxide: further evidence for a benzodiazepine spinal analgesic effect. European Journal of Anaesthesiology 8:227-231, 1991.

Goodchild, CS. Total intravenous anaesthesia for the high risk patient, Total Intravenous Anaesthesia. Edited by Kay B. Amsterdam, Elsevier, 1991.

Goodchild CS. Can Benzodiazepines provide anaesthesia? (a) Why give midazolam spinally? Bailieres Clinical Anaesthesiology, International Practice and Research. Intravenous Anaesthesia - What is New? Edited by Dundee JW, Sear JW. London, Bailliere Tindall, 1991, pp 361-369.

Goodchild CS : Cardiovascular Effects of Propofol and Relevance to Use in Patients with Compromised Cardiovascular Function. Semin Anesth 1991.

Goodchild CS, Sanghera S, Serrao JM, Gent JP. Analgesia mediated by spinal K-opioid receptors. European Journal of Anaesthesia 8:227-231, 1991.

Serrao NM, Marks RL, Morley SJ, Goodchild CS. Intrathecal midazolam for the treatment of chronic mechanical low back pain: a controlled comparison with epidural steroid in a pilot study. Pain 48:5-12, 1992.

Goodchild CS. Spinal cord effects of drugs used in anaesthesia. General Pharmacology 23(6):1992.

Goodchild CS. Multiple modes of opioid administration: real or imagined advantages. Curr Opin Anaesth 4:535-539, 1992.

Goodchild CS. Effects of general anaesthetics and analgesics on spinal circuits, Neural Mechanisms of General Anaesthesia. Edited by Winlow W, Angel A. Manchester, Manchester University Press, 1992.

Goodchild CS. Multiple modes of opioid administration : real or imagined advantages, Current Opinion in Anaesthesiology: opioids and other analgesics. Edited by Pleuvry BJ. Current Science, 1992, pp 535-539.

Akhtar TM, Goodchild CS, Boylan MKG. Reversal of streptokinase-induced bleeding with aprotinin for emergency cardiac surgery. Anaesthesia 47:226-228,1992.

Orchard MA, Goodchild CS, Prentice CMR, Davies JA, Benoit SE, Creighton-Kemsford LJ, Gaffney PJ, Michelson AD. Aprotinin reduces cardiopulmonary bypass-induced blood loss and inhibits fibrinolysis without influencing platelets, 1993.

Goodchild CS. A fresh look at management of postoperative pain. Hospital Update 1993.

Goodchild CS. Acute Postoperative Pain: Logical treatment by drug combinations. British Journal of Theatre Nursing 2:15-19, 1993.

Goodchild CS. Non-opioids and spinal analgesia. Anaes Pharm Rev 2:184-192, 1993.

Goodchild CS. GABA receptors and benzodiazepines. British Journal of Anaesthesia. 71, 127-133, 1993.

Goodchild, CS. The use of non-steroidal analgesics - the current position. Anaesthesiology, 28-34, 1993.

Goodchild, CS. Animal Welfare Conference Proceedings, Monash University Ethics, "Analgesics to use or not to use, that is the question", CS Goodchild, 13-14 May, 1993, pp34-35.

Barnes R, Rosenfeld J, Fennessy S, Goodchild C. Continuous subarachnoid infusion to control severe cancer pain in an ambulant patient. The Medical Journal of Australia. 1994.

Goodchild CS, Guo A, Davies A, Gent JP. Antinociceptive actions of intrathecal xylazine: interactions with spinal cord opioid pathways. British Journal of Anaesthesia, 76: 544-551, 1996.

Goodchild CS, Guo Z, Musgreave A, Gent JP. Antinociception by intrathecal midazolam involves endogenous neurotransmitters acting at spinal cord delta opioid receptors. British Journal ofAnaesthesia 77: 758-763, 1996.

Nadeson R, Guo Z, Porter V, Gent JP, Goodchild CS. γ-Aminobutyric Acid$_A$ receptors and spinally mediated antinociception in rats. The Journal of Pharmacology and Experimental Therapeutics, 278:2, 620-626, 1996.

Turner G, Blake D, Buckland M, Chamley D, Dawson P, Goodchild C, Mezzatesta J, Scott D, Sultana A, Walker S, Hendrata M, Mooney P, Armstrong M. Continuous extradural infusion of ropivacaine for prevention of postoperative pain after major orthopaedic surgery. British Journal of Anaesthesia, 76: 606-610, 1996.

Goodchild CS, Guo Z, Freeman J, Gent JP. 5-HT spinal antinociception involves mu opioid receptors: cross tolerance and antagonist studies. British Journal of Anaesthesia, 78: 563-569, 1997.

Goodchild CS. Nonopioid spinal analgesics: animal experimentation and implications for clinical developments. Pain Reviews, 4: 33-58, 1997.

Nadeson R, Goodchild CS. Antinociceptive properties of propofol: involvement of spina cord γ-aminobutyric acid$_A$ receptors. Journal of Pharmacology and Experimental Therapeutics 283: 1181-1186, 1997.

Monagle J, Barnes R, Goodchild C, Hewitt M. Ondansetron is not superior to moderate dose metoclopramide in the prevention of post-operative nausea and vomiting after minor gynaecological surgery. European Journal of Anaesthesiology, 14: 604-609, 1997.

Howe PW, Condon JR, Goodchild CS. Anaesthesia for aboriginal Australians. Anaesthesia and Intensive Care, 26(1): 86-91, 1998.

Chow TKF, Penberthy A, Goodchild CS. Ketamine as an adjunct to morphine in post-thoracotomy

analgesia: an unintended N-of-1 study. Anesthesia and Analgesia, 87(6) p1372-1374, 1998

Penberthy AJ, Goodchild CS. Undergraduate education in critical care. Anaesthesia and Intensive Care. 27(3) 314, 1999.

Goodchild CS. Spinal gaba system : target for new analgesics. Regional Anaesthesia and Pain Management Current Perspectives. 5th Bienniel Congress of AOSRA, 29 Oct-2 Nov 1999 ed. Dureja GP, Madan R, Kaul HL. New Delhi India, p31-36. 1999 ISBN 81 704 2156X.

Burmeister L, Tsaltas J, Goodchild CS, Mamers P, Healy DL. Randomised controlled trial of post operative pain and activity following microlaparoscopy and standard laparoscopy. Gynaecological Endoscopy. Vol 9, 41-45, 2000.

Penberthy AJ, Goodchild CS. Undergraduate education in critical care. Anaesthesia and Intensive Care. 27(3) 314, 1999.

Goodchild CS. Spinal GABA system : target for new analgesics. Regional Anaesthesia and Pain Management Current Perspectives. 5th Bienniel Congress of AOSRA, 29 Oct-2 Nov 1999 ed. Dureja GP, Madan R, Kaul HL. New Delhi India, p31-36. 1999 ISBN 81 704 2156X.

Burmeister L, Tsaltas J, Goodchild CS, Mamers P, Healy DL. Randomised controlled trial of post operative pain and activity following microlaparoscopy and standard laparoscopy. Gynaecological Endoscopy. Vol 9, 41-45, 2000.

Goodchild CS, Guo A, Nadeson R. Antinociceptive properties of neurosteroids I: Spinally mediated antinociceptive effects of water-soluble aminosteroids. PAIN 88: p23-29, 2000

Nadeson R, Goodchild CS. Antinociceptive properties of neurosteroids II: Experiments with Saffan and its components alphaxalone and alphadolone to reveal separation of anesthetic and antinociceptive effects and the involvement of spinal cord $GABA_A$ receptors. PAIN 88 : 31-39, 2000

Nadeson R, Goodchild CS. Antinociceptive properties of neurosteroids III: Experiments with alphadolone given intravenously intraperitoneally and intragastrically. British Journal of Anaesthesia, 86(5) : 1-5, 2001

Goodchild CS, Robinson A, Nadeson R. Antinociceptive properties of neurosteroids IV: A prospective randomised placebo controlled phase 1 study demonstrating the analgesic effects of alphadolone administered orally to humans. British Journal of Anaesthesia 86(4) :528-34, 2001

Zurek, JR, Nadeson R, Goodchild CS. Spinal and supraspinal components of opioid antinociception in streptozotocin induced diabetic neuropathy in rats. PAIN 90: 57-63, 2001

Wadhwa A, Clarke D, Goodchild CS High dose oral dextromethorphan as an adjunct to patient controlled analgesia with morphine after knee surgery. Anesthesia and Analgesia 92: 448-54, 2001.

Nadeson R, Goodchild CS The antinociceptive role of 5-HT1 receptor subtypes in rat spinal cord. British Journal of Anaesthesia 88(5) 679-684. 2002

Goodchild CS, Nadeson R, Tucker A, Bajunaki E. Potentiation by ketamine of fentanyl antinociception 1: An experimental study in rats showing that ketamine administered by non-spinal routes targets spinal cord antinociceptive systems. British Journal of Anaesthesia 88(5) 685-691, 2002

Lograsso M Nadeson R Goodchild C The spinal antinociceptive effects of cholinergic drugs in rats : receptor subtype specificity in different nociceptive tests. BioMed Central Pharmacology 2:20, 1471-2210, 2002

Winter L, Nadeson R, Tucker A, Winter L, Goodchild CS Antinociceptive properties of neurosteroids V: a comparison of alphadolone and alphaxalone in potentiation of opioid antinociception Anesthesia & Analgesia, 97: 798-805, 2003

Shah F, Halbe A, Panchal I, Goodchild CS Improvement in posteroperative pain relief by the addition of midazolam to an intrathecal injection of buprenorphine and bupivacaine European Journal of Anaesthesiology 20: 904-910, 2003

Goodchild Cs, Nadeson, R Cohen E. Spinal cord opioid receptors responsible for antinociception following intrathecal morphine injections. European Journal of Anaesthesiology 21(3): 179-85, 2004

Tucker A, Lai C, Nadeson R, Goodchild CS. Intrathecal midazolam I: A cohort study investigating safety. Anesthesia and Analgesia June 2004

Tucker A, Mezzatesta J, Barr H, Nadeson R, Goodchild CS Intrathecal midazolam II: Combination with intrathecal fentanyl for labour pain. Anesthesia & Analgesia in press June 2004

Goodchild C, Chow T, To E, McNeil J A simple fast east method to identify the evidence base in pain relief research: validation of a computer search strategy used alone to identify quality randomised controlled trials. Anesthesia & Analgesia June 2004

Good P, Tullio F, Jackson K, Ashby M, Goodchild CS, Short term 'Burst' subcutaneous triple-agent infusions of Ketamine combined with an opioid and anti-inflammatory agent for episodes of acute or chronic pain. Internal Medicine Journal inpress 2004

Chapters published:

Goodchild CS, Serrao JM. Analgesics and the spinal cord dorsal horn. In: Kaufman, L (ed). Anaesthesia Review 6, pp 215-229. London: Churchill Livingstone, 1989

Goodchild CS, Jones JG. Opioid antagonists. In: Current Opinion in Anaesthesiology, vol.3(4), pp.601-606, 1990.

Goodchild CS. Total intravenous anaesthesia in the high risk patient. In: Kay, B (ed). Total Intravenous Anaesthesia, pp.351-359. Amsterdam: Elsevier Science Publications, 1991.

Goodchild CS. Why give midazolam spinally? In: Dundee & Scar (eds) Intravenous Anaesthesia - What is New?", 1991.

Goodchild CS. Cardiovascular effects of propofol and relevance to use in patients with compromised cardiovascular function. In: Seminars in Anaesthesia, 1991.

Goodchild CS. Benzodiazepines. General Anaesthesia, 6th edition, 1994.

Goodchild CS. Principles of Anaesthesia: pain management and respiratory management in surgery. In: Scott: An Aid to Clinical Surgery, Churchill Livingstone, London, ISBN 044305603X 6th ed. 1998: 6-13.

Theses of Past Students of Monash University Dept Anaesthesia

Kavenagh, Jane A. Investigation of $GABA_A$ receptors involved in spinal antinociception. Hons 1995

Zurek, James R. The antinociceptive effect of opioids in a model for diabetes-induced neuropathic pain. Hons 1996

Lograsso, M. The spinal antinociceptive effects of cholinergic drugs in rats. Hons 1998

Bajunaki, Edna. The spinal antinociceptive effect of ketamine in acute pain models in rats. Hons 1999

Fleming, Julia. Spinal cord $GABA_A$ and benzodiazepine receptors modulating nociception. PhD 2000

Winter, Lara Potentiation of Opioid antinociception by the Neurosteroid analgesic alphadolone, Hons 2000; PhD thesis submitted March 2004

Testa, Isabelle Hons 2000

Tucker, Adam PhD 2001

Patents

Australia 698746 New use of pregnane-diones as analgesics Goodchild
Australia 735092 New use of pregnane-diones as analgesics Goodchild
USA 6048848 New use of pregnane-diones as analgesics Goodchild

PRESENTATIONS DURING CURRENT APPOINTMENT

International:

XII International Congress of Pharmacology, Montreal, 24-29 July, 1994. Spinal Antinociceptive actions of ORG 20380, a water soluble steroid anaesthetic, CS Goodchild.

1st Meeting of the Japanese Society for Intravenous Anaesthesia and Infusion Technology, Tokyo, 25 November, 1994. Clinical benefit of intravenous anaesthesia – compared with that of inhalational anaesthesia. CS Goodchild.

Australasian Society of Clinical and Experimental Pharmacology and Toxicology, Auckland, December 1994. Alphaxalone / alphadolone a steroid anaesthetic combination (SAFFAN) produces antinociception at sub anaesthetic doses: evidence for spinally-mediated antinociception by neuroactive steroids in rats. R Nadeson CS Goodchild.

12th World Congress International Federation of Physical Medicine and Rehabilitation, Sydney, 28 March, 1995. Symposia 1 – Session 2 Pain and Neurotransmitters Co-Chairperson CS Goodchild.

12th World Congress International Federation of Physical Medicine and Rehabilitation, Sydney, 28 March, 1995. GABA and NMDA in spinal antinociception. CS Goodchild.

17th Annual Meeting of the European Academy of Anaesthesiology, Helsinki, 24-27 August, 1995. Continuous epidural infusion of ropivacaine 0.2% for the prevention of postoperative pain after major orthopaedic surgery; a volume response study. Goodchild CS, Blake DW, Buckland M, Scott DA, Turner G, Walker S.

17th Annual Meeting of the European Academy of Anaesthesiology, Helsinki, 24-27 August, 1995. Interactions of intravenous anaesthetic agents and spinal cord antinociceptive systems: investigations of the actions of propofol and the neurosteroid anaesthetic combination saffan with spinal cord $GABA_A$ receptors. Goodchild CS. Nadeson R.

11th World Congress of Anaesthesiologist, Sydney, 14-20 April, 1996. Chairperson – Analgesic Pharmacology. CS Goodchild.

11th World Congress of Anaesthesiologist, Sydney, 14-20 April, 1996. Chairperson – Analgesic posters. CS Goodchild.

11th World Congress of Anaesthesiologists, Sydney, 14-20 April 1996. Auditing anaesthetic and post operative pain relief services. D1361 Goodchild CS.

11th World Congress of Anaesthesiologists, Sydney, 14-20 April 1996. Spinal effects of intrathecal fentanyl in a rat chronic pain model. P354 AP Anderson, CS Goodchild .

11th World Congress of Anaesthesiologists, Sydney, 14-20 April 1996. Non sedating doses of propofol produce antinociception by the same spinal mechanism responsible for intrathecal midazolam antinociception. D317. R Nadeson, CS Goodchild.

8th World Congress on Pain, Vancouver, Canada, 17-22 August 1996. Effects of intrathecal 5-HT in a rat neuropathic pain model. A73 . Anderson A, Goodchild CS.

8th World Congress on Pain, Vancouver, Canada, 17-22 August 1996. Non sedating doses of propofol produce antinociception by the same spinal mechanism responsible for intrathecal midazolam antinociception. A94 . R Nadeson, CS Goodchild.

Korean Pain Society, Seoul. Non opioid spinal analgesia, 22-23 November, 1997. CS Goodchild.

Indian Society for Study of Pain, Bombay, 27 May, 1998. Intrathecal drugs. CS Goodchild.

Indian Society of Anaesthetists, Bombay, 13 June, 1998. Pain management – different modes, CS Goodchild.

Royal College of Anaesthetists, Scientific Meeting, London, 5-6 November, 1998. Spinal analgesic drugs: Mechanism of action. CS Goodchild.

An oblique saggital spinal cord slice preparation for the study of nociceptive transmission in the adult rat. 9th World Congress on Pain, Vienna Austria 22-27 Aug 1999. AJ Penberthy, CS Goodchild

Creating a database of double blinded randomised controlled trials in pain research with Strategy-DR. 9th World Congress on Pain, Vienna Austria 22-27 Aug 1999 T Chow, E To, CS Goodchild, JJ McNeil

How to introduce a new local anaesthetic in clinical practice. AOSRA New Delhi India 29 Oct-2 Nov 1999 Goodchild, CS

Spinal GABA System – target for new analgesics AOSRA New Delhi India 29 Oct-2 Nov 1999 Goodchild CS

Role of Intrathecal drugs in pain management. Global Update on Pain and XVth National Conference of

Indian Society for Study of Pain 11-13 February 2000. Bombay India. CS Goodchild

Spinal cord opioid receptors responsible for antinociception following morphine injections in rats. Joint Meeting Australiasian Society of Clinical and Experimental Pharmacologists and Toxicologists and British Pharmacological Society. 26 – 28 April 2000 Oral 13-6. Nadeson R, Cohen E, Goodchild CS.

Antinociceptive properties of neurosteroids: preclinical studies. P3 12th World Congress of Anaesthesiologists. Book of Abstracts. Montreal Canada 4-9 June 2000. Goodchild CS Nadeson R.

Improved indexing of randomised controlled trials has enabled computer search strategies to identify them with high sensitivity and specificity, in pain relief research. 8th International Cochrane Colloquium, Capetown South Africa 25-29 October 2000. Chow T To E, Goodchild C, McNeil J

Spinally administered non-opioid analgesics (clonidine, neostigmine, adenosine) the evidence. 6th biennial congress Asian & Oceanic Society of Regional Anesthesia. Oct 4-7 2001 Seoul, Korea Goodchild CS

Neurosteroids: A new class of analgesic. 6th biennial congress Asian & Oceanic Society of Regional Anesthesia. Oct 4-7 2001 Seoul, Korea Goodchild CS

National:

Australian Pain Society, Melbourne, 18 February, 1993. Around the horn. CS Goodchild.

Australian Society of Anaesthetists, Swan Hill , 24 April, 1993. Analgesics on the move. CS Goodchild.

ANZCA, 14 August, 1993. Anaesthesia for the elderly. CS Goodchild.

Australian Society of Anaesthetists, Perth, 23-27 October, 1993. TIVA. CS Goodchild.

National Hospice and Palliative Care Conference, Melbourne, 27-29 October, 1993. The use of benzodiazepines as analgesics, CS Goodchild.

ANZCA, Victorian Regional Committee, 10 February, 1994. Induction Agents Volatile Anaesthetics. CS Goodchild.

ANZCA, Academic Anaesthesia in Australia Symposium 19 February, 1994. What do you do with a new department? CS Goodchild.

ANZCA, Special Interest Group, Lorne, 5-6 March, 1994. Peripheral mechanisms of nociception. CS Goodchild.

Australian Pain Society, XVth Annual Scientific Meeting, Brisbane, 6-9 April 1994. Spinal antinociceptive actions of ORG 20380: A water soluble steroid anaesthetic, CS Goodchild

ANZCA, Annual Scientific Meeting, Launceston, 1-5 May, 1994. Peripheral mechanisms of nociception. CS Goodchild.

Combined ANZCA/ASA Continuing Medical Education, Melbourne 13 August 1994. Concurrent drug therapy. CS Goodchild.

S.A. ANZCA / ASA Continuing Medical Education Committee, Adelaide, 20-21 August, 1994. Total

intravenous anaesthesia and balanced general anaesthesia still a useful concept? CS Goodchild.

Australian Neuroscience Society, 15th Annual Meeting University of Western Australia February. Sub-anaesthetic doses of propofol produce spinally-mediated antinociception in rats Oral 15-3. 1995 Nadeson R, Goodchild CS.

Australian Neuroscience Society, 15th Annual Meeting University of Western Australia February, 1995. Spinal effects of intrathecal fentanyl in a rat chronic pain model. Oral 15-4 Anderson AP, Goodchild CS.

Australian Society Anaesthetists, WA Section, Perth, 4-5 March, 1995. Acute pain management. CS Goodchild.

ANZCA Annual Scientific Meeting, Townsville, Queensland, 5-10 May 1995. Spinal effects of intrathecal fentanyl in a rat chronic pain model. AP Anderson, CS Goodchild

ANZCA Annual Scientific Meeting, Townsville, Queensland, 5-10 May 1995. Sub-anaesthetic doses of propofol produce spinally mediated antinociception in rats. R Nadeson, CS Goodchild

Australian Society of Anaesthetists, Radisson, Melbourne, 22 October, 1995. $GABA_A$ receptors – their relationship to anaesthesia and analgesia. CS Goodchild.

Australasian Society of Clinical and Experimental Pharmacology and Toxicology, Adelaide, December 1995. Investigation of $GABA_A$ receptor subtypes involved in spinal antinociception in rats. J Kavenagh, R Nadeson, CS Goodchild.

Australian Society of Anaesthetists, Melbourne, 18 February, 1996. Lecture. CS Goodchild.

Australian Pain Society, 17th Annual Scientific Meeting, Canberra, 10-13 March, 1996. Politics of pain. CS Goodchild.

Australian Orthopaedic Association, 23 September, 1996. Conservative Management of spinal pain. CS Goodchild.

ANZCA and ASA, Perth 26-30 October, 1996. Lecture. CS Goodchild.

Combined ASCEPT & APPS Meeting, Sydney, Australia, December 1996. Autoradiographic evidence that propofol and anaesthetic steroids increase [^{3}H]-muscimol and [^{3}H]-flunitrazepam binding in regions of rat and primate spinal cord that modulate nociception. Oral 15-5. JA Fleming, DI Finkelstein, CS Goodchild, B Jarrott

Combined ASCEPT & APPS Meeting Sydney, Australia, December 1996. Antinociceptive effects of an opioid (fentanyl) in a diabetic induced neuropatic pain model. Oral 1-4. J Zurek, R Nadeson, CS Goodchild.

Combined ASCEPT & APPS Meeting Sydney, Australia, December 1996. The effects of the steroid anaesthetics ORG 20549, ORG20380, ORG21047 and ORG20599 on spinal cord $GABA_A$ receptors. Oral 15-7 CS Goodchild.

Combined ASCEPT & APPS Meeting Sydney, Australia, December 1996. Anatomical characterization of adult rat spinal cord slice. Poster 11. AJ Penberthy, R Nadeson, CS Goodchild.

Combined ASCEPT & APPS Meeting Sydney, Australia, December 1996. Effects of intrathecal 5-HT in

a rat neuropathic pain model. Oral 0-5. A Anderson, R Nadeson, CS Goodchild.

Combined ASCEPT & APPS Meeting Sydney, Australia, December 1996. Spinal antinociception mediated by the $GABA_A$ receptor is activated by propofol. Oral 15-6. R Nadeson, CS Goodchild.

Australian Neuroscience Society 17th Annual Meeting, University of Newcastle, Feb 2-5, 1997. $GABA_A$ $receptor_{\alpha 1}$ –subunit expression in lumbar spinal cord of sciatic nerve injured and sham operated rats. Poster 4-20. JA Fleming, N Nichols, AJ Lawrence, B Jarrot, CS Goodchild.

Australian Neuroscience Society 17th Annual Meeting University of Newcastle, Feb 2-5, 1997. Spinal $GABA_A$ receptors as targets for analgesics. CS Goodchild.

ANZCA, Annual Scientific Meeting, Christchurch, 10-14 May, 1997. Propofol and spinally mediated antinociception. CS Goodchild

Australian Society of Anaesthetists, Hobart, 23-27 October, 1997. Chairperson – Drugs in Anaesthesia. CS Goodchild.

ANZCA, Melbourne, 2 December, 1997. Update on spinal non opioid analgesics. CS Goodchild.

ANZCA, Annual Scientific Meeting, Newcastle, 2-5 May, 1998. Spinal cord glia and neurosteroid after peripheral nerve injury: a target for intrathecal midazolam? J Fleming, Lawrence AJ, Jarrot B, Goodchild CS.

ANZCA Annual Registrars' Scientific Meeting. Melbourne, 18 July, 1998. A systematic review of NSAIDs in post thoracotomy analgesia (1966-1998), T Chow , CS Goodchild, E To.

ASTRA Clinical Meeting, Adelaide, 22 July, 1998. Prevention of post operative chronic pain – the role of the surgeon and anaesthetist. CS Goodchild.

ANZCA, Acute Pain Special Interest Group Meeting, Leura NSW, 25-26 July, 1998. Novel epidural analgesic drugs, CS Goodchild.

Australian Orthopaedic Association, Orthopaetic Training Program. Melbourne, 27 July, 1998. Conservative management of spinal pain. CS Goodchild.

ANZCA/ASA CME meeting Pain Medicine and the Anaesthetist 3 October 1998 Melbourne VIC. Intravenous epidural how when and why. CS Goodchild.

The antinociceptive role of 5-HT receptor subtypes in rats. ASCEPT 32nd Annual Scientific Meeting Hobart TAS Oral 1-1, 1998 Nadeson R, Goodchild CS

The spinal antinociceptive effects of cholinergic drugs in rats. ASCEPT 32nd Annual Scientific Meeting Hobart TAS Oral 1-2, 1998 Lograsso M, Goodchild CS, Nadeson R

What does $GABA_A$ receptor offer in pain relief? ANZCA Annual Scientific Meeting 8-12 May 1999, Adelaide. SA Pain Medicine Session. Goodchild CS.

Intrathecal midazolam in man: an audit of clinical practice to address issues of safety and side effects. ANZCA Annual Scientific Meeting 8-12 May 1999, Adelaide. SA Lai C, Tucker A, Nadeson R, Goodchild CS

Changes in spinal cord $GABA_A$ and benzodiazepine receptors following a chronic constriction injury of the sciatic nerve in the rat: implications for neuropathic pain states. Australian Society of Anaesthetists National Scientific Congress 23-27 October 1999 Cairns QLD Fleming, J, Nadeson R, Anderson A, Nichols N, Lawrence A, Jarrot B, Goodchild CS.

Interactions of anaesthetic agents with $GABA_A$ receptors in the rat and primate spinal cord. Australian Society of Anaesthetist National Scientific Congress 23-27 October 1999 Cairns QLD. Fleming J, Finklestein D, Goodchild CS, Jarrott B.

The antinociceptive effect of ketamine in acute pain models in man. ASCEPT. 33rd Annual Scientific Meeting 4-8 Dec 1999. Sydney NSW. Tucker A, Kim YI, Nadeson R, Goodchild CS.

The antinociceptive effect of ketamine in acute pain models in rats. ASCEPT. 33rd Annual Scientific Meeting 4-8 Dec 1999. Sydney NSW. Bajunaki E, Tucker A, Nadeson R, Goodchild CS

Resistance to the antinociceptive action of intrathecal midazolam in a model of neuropathic pain in the rat. Australia New Zealand College of Anaesthetists ASM. 6-10 May 2000, Melbourne Nadeson, R, Fleming J, Anderson A, Goodchild CS

.High dose dextromethorphan as an adjunct to analgesia with morphine after knee surgery. Australia New Zealand College of Anaesthetists ASM. 6-10 May 2000, Melbourne Wadhwa, A, Clarke D, O'Flaherty M, Goodchild CS

The effect of adding ketamine to intravenous PCA morphine after hysterectomy. Australia New Zealand College of Anaesthetists ASM. 6-10 May 2000, Melbourne Barnes, R, Fock, A Tucker A, Goodchild CS

Spinal cord opioid receptors responsible for antinociception following morphine injections in rats. Australia New Zealand College of Anaesthetists ASM. 6-10 May 2000, Melbourne Cohen E, Nadeson R, Bajunaki E Goodchild CS.

Intrathecal midazolam for analgesia: a survery of 1000 patients to search for neurological sequelae. Australia New Zealand College of Anaesthetists ASM. 6-10 May 2000, Melbourne Tucker, A, Nadeson R, O'Flaherty, M, Goodchild CS

The antinociceptive effect of ketamine in acute pain models in rats. Australia New Zealand College of Anaesthetists ASM. 6-10 May 2000, Melbourne Bajunaki, E, Nadeson R, Tucker A, Goodchild CS.

The antinociceptive effect of ketamine in acute pain models in humans. Australia New Zealand College of Anaesthetists ASM. 6-10 May 2000, Melbourne Tucker A, Yong Ik Kim, Nadeson R, Goodchild CS

Potentiation of opioid antinociception by the neurosteroid analgesic alphadolone. Proceedings of ASCEPT 2000. The Australian Society of Clinical and Experimental Pharmacologists and Toxicologists, 34th ASM Newcastle. 3-6 December 2000 Winter L, Nadeson R, Tucker A, Goodchild CS.

The interaction between opioids and benzodiazepines in producing spinal antinociception. Proceedings of ASCEPT 2000. The Australian Society of Clinical and Experimental Pharmacologists and Toxicologists. 34th ASM Newcastle 3-6 December 2000. Testa I, Nadeson R, Tucker A, Goodchild CS.

Neurosteroid the magic bullet has arrived. Combined ANZCA/ ASA state Scientific Meeting Feb 17-18, 2001 Coles Bay Tasmania Goodchild CS

Antinociceptive properties of neurosteroids: experiments with alphadolone showing potentiation of the

antinociceptive effects of opioids. ANZCA and Hong Kong College of Anaesthesiologists combined CSM May 5-9 2001 Hong Kong Winter L, Nadeson R, Tucker A, Goodchild CS.

The interactions between opioids and benzodiazepines in spinal antinociception. ANZCA and Hong Kong College of Anaesthesiologists combined CSM May 5-9 2001 Hong Kong Nadeson R, Testa I, Tucker A, Goodchild CS

Computer search strategies are efficient in identifying the quality randomised controlled trials in pain relief research. ANZCA and Hong Kong College of Anaesthesiologists combined CSM May 5-9 2001 Hong Kong Chow T, To E, Goodchild C, McNeil J.

Normal opioid sensitivity is restored in streptozotocin induced diabetic neuropathy by the neurosteroid analgesic alphadolone. 23rd ASM Australian Pain Society, 24-27 March, 2002 CS Goodchild

Alphadolone potentiation of opioid antinociception: an interaction at spinal cord GABAA receptors. 23rd ASM Australian Pain Society, 24-27 March, 2002 L Winter, R Nadeson, J Han, CS Goodchild

Goodchild CS, Winter L Alphadolone potentiation of opioid antinociception: an interaction at spinal cord $GABA_A$ receptors.IASP 10th World Congress on Pain Aug 17-22 2002 SanDiego USA

L Winter, R Nadeson, J Han, CS Goodchild Alphadolone potentiation of opioid antinociception: an interaction at spinal cord $GABA_A$ receptors. 23rd ASM Australian Pain Society, 24-27 March, 2002

Shah, F Halbe, A Panchal I, Goodchild C Improvement in postoperative pain relief by the addition of midazolam to an intrathecal injection of buprenorphine and bupivacaine. ANZCA ASM Hobart 3-6 May 2003

A Tucker, R Nadeson, C Goodchild, I Testa The interaction of midazolam and fentanyl in relation to an antinociceptive response surface. ANZCA ASM Hobart, 3-6 May 2003

A Tucker, Malkoutzis V, J Mezzatesta, V Thomas, D Castanelli, R Nadeson, C Goodchild Intrathecal midazolam does not potentiate the effect of morphine on postoperative caesarian section pain. ANZCA ASM Hobart, 3-6 May 2003

A Tucker, J Mezzatesta, H Barr, R Nadeson, C Goodchild Intrathecal midazolam potentiates the effect of fentanyl on labour pain. ANZCA ASM Hobart, 3-6 May 2003

Goodchild C, What are the potential uses for ketamine analgesia? ASA Melb 1-4 Oct 2003.

Goodchild C Introductory Remarks to Scientific Programme – Acute Pain SIG and ANZCA Faculty of Pain Medicine CME 30 Sep-1 Oct 2003

Goodchild C MODERATOR Patients across boundaries discussion group – Acute Pain SIG and ANZCA Faculty of Pain Medicine CME 30 Sep-1 Oct 2003

Jackson K Goodchild C, Ashby M, Domicillary Use of patient administered intranasal analgesia to cover painful dressings over many months: a case review. 2003

Ashby, M Jackson K, Goodchild C, Is short term sub-anaesthetic dose ketamine on the way to being a front-line analgesic? Clinical and research experience at MMC. 2003

Winter L Nadeson R Goodchild CS, The analgesic neurosteroid alphadolone can reverse hyperalgesia in

carrageenan inflammation. ASCEPT Sydney 1-3 Dec 2003

Han CC, Nadeson R Winter L, Goodchild CS, Improvement of the antinociceptive effects of tramadol by co-administration with the analgesic neurosteroid alphadolone. ASCEPT Sydney 1-3 Dec 2003

Goodchild, CS Spinal Gabaergic mechanisms and their implications for analgesic action. ANS Melbourne, 28-30 Jan 2004

Others:

Animal Welfare Conference, Monash University, 13-14 May 1993. Analgesics: to use or not to use, that is the question. CS Goodchild.

Anaesthetic Department Alfred Hospital, 20 May, 1993. Neurosteroids. CS Goodchild.

Anaesthetic Department St Vincents Hospital, 2 July, 1993. Neurosteroids. CS Goodchild.

Annual Clinical Meeting, Mercy Private Hospital, 6 October, 1993. Pain and its management, CS Goodchild.

Pharmacology Department, Monash University, 14 October, 1993. GABA – potential for neuroanalgesic development, CS Goodchild.

Anaesthetic Group, Wangaratta, 5-6 November, 1993. Lecture. CS Goodchild.

Prince Henry's Institute Medical Research, Melbourne, 12 November, 1993. Neurosteroids and analgesia, CS Goodchild.

Emergency Nurses Association Conference, Melbourne, 13 November, 1993. Analgesia on the move, CS Goodchild.

Dandenong Hospital/ICI, 9 December, 1993. Total anaesthesia for the high risk patient. CS Goodchild.

ICI Anaesthetic Meeting, ICI House Melbourne, 11 & 18 November 1993. Total intravenous anaesthesia. CS Goodchild.

Anaesthetic Department, Frankston Hospital, 20 May, 1994. Lecture. CS Goodchild,

Medical Research dinner, Hyatt 23 June, 1994. Lecture. CS Goodchild.

Anaesthetic Department, Box Hill Hospital 21 July, 1994 . Lecture. CS Goodchild.

ICI, Caulfield Race Course, 30 August, 1994. Clinical application of anaesthetic maintenance with propofol. CS Goodchild.

Update for GPs, Monash University Medical School, 25 October, 1994. Pain management – practical guidelines for common painful conditions. CS Goodchild.

Anaesthetic Department Geelong, 28 February, 1995. TIVA with propofol. CS Goodchild.

Animals in Science Conference. Perspectives on their use, care and welfare. Monash University Victoria, 19-21 April 1995. Analgesic effects of veterinary anaesthetic drugs. 66P. CS Goodchild.

Peter MacCallum Cancer Institute Grand Round, 22 May 1995. Rats to man in one jump. CS Goodchild.

Anaesthetic Group, Wangaratta, 3 November, 1995. Lecture. CS Goodchild.

Glaxo Anaesthetic Meeting, Marchettis, Melbourne. 14 November, 1996. Lecture. CS Goodchild.

Post Operative Pain Management Symposium, Hyatt, Melbourne, 3 March, 1997 CS Goodchild.

Mini Symposium, Mercy Private and Monash Medical Centre, Melbourne. 2-3 May, 1997. Scientific activities of Monash University Department of Anaesthesia. J Fleming, CS Goodchild, R Nadeson.

Anaesthetic Education Meeting, Melbourne, 1 October, 1997. Operative use of anaesthetics: relationship to post operative pain. CS Goodchild.

Anaesthetic Lecture, Astra, Melbourne, 18 November, 1997 Management of acute pain : relevance to chronic pain. CS Goodchild.

Anaesthetic Academic Meeting, Southern Health Care Network, 14 March, 1998. Post marketing surveillance studies Strom, CS Goodchild.

Anaesthetic Academic Meeting, Southern Health Care Network, 14 March, 1998. Intrathecal analgesia. CS Goodchild.

The Victorian Society of Post Anaesthesia and Anaesthesia Nurses. Melbourne, 19-20 June 1998. A simple strategy (strategy-Dr) to identify randomised trials in post operative research. T Chow, CS Goodchild.

ANZCA Victorian Regional Committee Annual Anaesthetic Registrar's Scientific Meeting 18 July 1998 Melbourne A systematic review of NSAIDS in post-thoracotomy analgesia (1966-1998) TFK Chow, CS Goodchild, E To.

Clinical meeting ASTRA 22 July 1998 Adelaide SA. Prevention of post operative chronic pain -- the role of the surgeon and anaesthetist. CS Goodchild

Annual Clinical Anaesthetic Meeting Valley Private Hospital Melbourne. New Directions in perioperative pain control 10 September 1998 CS Goodchild.

Peninsula and Southern Health Care Network Academic Meeting, 18 September, 1998. Intrathecal Infusion. CS Goodchild.

Anaesthetic Meeting 21 September 1998. St Vincents Hospital Melbourne. Advantages of ketamine for post operative pain relief. CS Goodchild

Surgical Audit and Forum Program. March 16 1999. Monash Medical Centre. Pain Management. CS Goodchild.

Monash / Mercy Anaesthesia Meeting. 10 April 1999 Monash Medical Centre. Analgesia Review -- New Advances. CS Goodchild

Monash Training Day 1st Part and HMO Teaching. 22 June 1999 Monash Medical Centre. Pain --

Applying the Basic Sciences. CS Goodchild.

Pain Management Day. 26 July 1999 Cabrini Hospital. Pain management lecture CS Goodchild

Cystic Fibrosis Seminar. 27 July 1999 Monash Medical Centre Chronic Pain in cystic fibrosis. CS Goodchild.

Monash Training Scheme 2nd Part Registrar Tutorials. July 28 1999 Monash Medical Centre. Pain. CS Goodchild.

Surgery for Lawyers "Advanced symposium on controversy". 11 November 1999. Multidisciplinary pain management: needles and pins. CS Goodchild

Lecture – Grad Dip Nursing (Perioperative) - Pain Management. April 11, 2000 Deakin University. CS Goodchild

Neurosteroids in Pain, St Vincents Hospital, Anaesthetic Department meeting, 14 March 2001 CS Goodchild

Pain Lecture, The University of Queensland School of Pharmacy 3 May 2001 CS Goodchild

Neurosteroid Analgesia, 29 August 2001 Palliative Medicine Committee (subcommittee of Victorian Cooperative Oncology Group), Anti-Cancer Council of Victoria. CS Goodchild

Lecture, Victorian Neuroscience Group 1 May 2002 CS Goodchild

Educational Lecture, Valley and South Eastern Private Hospital 7 May 2002 CS Goodchild

Pain lecture - ANZCA primary tutorial 27 May 2002 CS Goodchild

CSL National Cycle Meeting, Hamilton Island 4-8 Aug 2002 L Winter

Neurosciences Victoria Drugs targeting spinal cord $GABA_A$ receptors: the magic bullet has arrived. 11 August 2003 CS Goodchild